Exhibit 2

UNITED STATES DEPARTMENT OF COMMERCE
Patent and Trademark Office

Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

SERIAL NUMBER	FILING DATE	FIRST NAMED APPLICANT	ATTORNEY DOCKET NO.
06/760,236	07/29/85	GOODMAN	

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EXAMINER	
FOX, D	
ART UNIT	PAPER NUMBER
127	7

DATE MAILED: 06/09/87

This is a communication from the examiner in charge of your application.

COMMISSIONER OF PATENTS AND TRADEMARKS

☑ This application has been examined ☑ Responsive to communication filed on 3/3/87 ☐ This action is made final.

A shortened statutory period for response to this action is set to expire 3 month(s), ____ days from the date of this letter. Failure to respond within the period for response will cause the application to become abandoned. 35 U.S.C. 133

Part I THE FOLLOWING ATTACHMENT(S) ARE PART OF THIS ACTION:

1. ☑ Notice of References Cited by Examiner, PTO-892.
2. ☐ Notice re Patent Drawing, PTO-948.
3. ☐ Notice of Art Cited by Applicant, PTO-1449
4. ☐ Notice of Informal Patent Application, Form PTO-152
5. ☐ Information on How to Effect Drawing Changes, PTO-1474
6. ☐ _____

Part II SUMMARY OF ACTION

1. ☑ Claims 1-13 are pending in the application.

   Of the above, claims _____ are withdrawn from consideration.

2. ☐ Claims _____ have been cancelled.

3. ☐ Claims _____ are allowed.

4. ☑ Claims 1-13 are rejected.

5. ☐ Claims _____ are objected to.

6. ☐ Claims _____ are subject to restriction or election requirement.

7. ☐ This application has been filed with informal drawings which are acceptable for examination purposes until such time as allowable subject matter is indicated.

8. ☐ Allowable subject matter having been indicated, formal drawings are required in response to this Office action.

9. ☐ The corrected or substitute drawings have been received on _____. These drawings are ☐ acceptable; ☐ not acceptable (see explanation).

10. ☐ The ☐ proposed drawing correction and/or the ☐ proposed additional or substitute sheet(s) of drawings, filed on _____. has (have) been ☐ approved by the examiner. ☐ disapproved by the examiner (see explanation).

11. ☐ The proposed drawing correction, filed _____, has been ☐ approved. ☐ disapproved (see explanation). However, the Patent and Trademark Office no longer makes drawing changes. It is now applicant's responsibility to ensure that the drawings are corrected. Corrections MUST be effected in accordance with the instructions set forth on the attached letter "INFORMATION ON HOW TO EFFECT DRAWING CHANGES", PTO-1474.

12. ☐ Acknowledgment is made of the claim for priority under 35 U.S.C. 119. The certified copy has ☐ been received ☐ not been received ☐ been filed in parent application, serial no. _____; filed on _____.

13. ☐ Since this application appears to be in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under Ex parte Quayle, 1935 C.D. 11; 453 O.G. 213.

14. ☐ Other

Exhibit 2

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The specification is objected to under 35 U.S.C. 112, first paragraph, as failing to provide an enabling disclosure.

The invention employs novel plasmids and microorganisms. Repeatability of the disclosed method and availability of starting materials is unclear; therefore a deposit should be made for enablement purpose.

Applicants may provide assurance of compliance with the requirements of §112 in the form of a declaration averring that (a) during the dependency of this application, access to the invention will be afforded to one determined by the Commissioner upon request, (b) all restrictions upon availibility to the public will be irrevocably removed upon granting of the patent and (c) the deposit will be maintained in a public depository for a period of 30 years or 5 years after the last request or for the effective life of the patent, whichever is longer. See MPEP 608.01(p)C.

Claims 1-13 are rejected under 35 U.S.C. 112, first paragraph, for the reasons set forth in the above objection to the specification.

Claims 1-5, 7, 8, 10 and 11 are rejected under 35 U.S.C. 112, first paragraph, as the disclosure is enabling only for claims limited to Agrobacterium-mediated dicot transformation with chimeric genes comprising opine synthase promoters and structural genes encoding human interferon or antibiotic resistance as per pages 10-18. See MPEP 706.03(n) and 706.03(z).

The specification only provides detailed experimental examples demonstrating dicot transformation using Agrobacterium. Other means of plant transformation are limited by lack of chromosomal incorporation of DNA and lack of plant regeneration from transformed protoplasts. Agrobacterium-mediated transformation is limited by host range and regenerability of transformed protoplasts to the dicots (Goodman et al. pages 52-53). Undue experimentation would be required by one of ordinary skill in the art to obtain non-Agrobacterium mediated transfer of monocots as claimed in claims 1 and 7.

Furthermore, the specification only provides detailed experimental examples demonstrating the expression of human interferon in plant cells regulated by opine synthase promoters. As admitted by Applicants (page 5 of Amendment filed on February 23, 1987) the ability of a given promoter to direct translation of a detectable amount of stable, bioactive, recoverable gene product is not predictable. For example, phaseolin

expression was virtually undetectable in transformed sunflower cells under phaseolin promoter regulation but was detected at significantly higher levels when regulated by the octopine synthase promoter (Murai et al, page 480, third column, first full paragraph). Given the unpredictability inherent in the art, undue experimentation would be required by one of ordinary skill in the art to determine DNA sequences for non-disclosed mammalian peptides or promoters and to develop transformation vectors resulting in detectable expression of stable, bioactive peptides as claimed in claims 1-5, 8, 10 and 11.

Claims 1-4, 6-8, 12 and 13 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1 and 7 are incomplete for failing to include the means of introducing the claimed integrated sequences into the plant cells. Claims 2, 6, 8 and 12 are indefinite in their recitation of "includes" or "including" as it is unclear whether this is an open or closed term. Claims 3 and 4 are confusing in their recitation of "said transcriptional and translational initiation region" for failing to distinguish between the regions of the first or second expression cassette.

Claims 3 and 7 are indefinite in their recitation of "derived ... from" which fails to adequately characterize the claimed regions. Claim 4 is indefinite for failing to employ proper Markush terminology. See MPEP 706.03y. Claim 13 is confusing in its recitation of "regulatory the expression of" as it is unclear what Applicants intend.

The following is a quotation of 35 U.S.C. 103 which forms the basis for all obviousness rejections set forth in this Office action:

> A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.
>
> Subject matter developed by another person, which qualifies as prior art only under subsection (f) and (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

Claims 1-4, 6-8 and 10-13 are rejected under 35 U.S.C. 103 as being unpatentable over Murai et al in view of Gray et al.

Murai et al. discloses the recovery of phaseolin from sunflower cells transformed with chimeric genes comprising structural genes encoding phaseolin and a

selectable antibiotic resistance enzyme regulated by octopine synthase promoters. Gray et al. discloses the recovery of biologically active human interferon from E. coli and monkey cells transformed with cDNA encoding interferon. In the absence of unexpected results it would be obvious to one of ordinary skill in the art to incorporate the interferon-encoding cDNA disclosed by Gray et al. into the plant transformation method disclosed by Murai et al to obtain the claimed methods and expression cassettes, since the disclosed plant transformation vectors and cDNA would continue to function in their known and expected manner.

Claim 5 is rejected under 35 U.S.C. 103 as being unpatentable over Murai et al in view of Gray et al as applied to claims 1-4, 6-8 and 10-13 above, and further in view of Herrera-Estella et al.

Murai et al taken in view of Gray et al discloses a method for recovering interferon from plants as discussed supra. Herrera-Estella et al. discloses plant transformation using the pea RUBISCO small subunit promoter to recover bacterial enzymes conferring antibiotic resistance. In the absence of unexpected results it would be obvious to one of ordinary skill in the art to incorporate the promoter disclosed by Herrera-Estrella et al. into the transformation method disclosed by Murai

et al taken in view of Gray et al, since the RUBISCO promoter would continue to function in its known and expected manner.

Claim 9 is rejected under 35 U.S.C. 103 as being unpatentable over Murai et al in view of Gray et al as applied to claims 1-4, 6-8 and 10-13 above, and further in view of Velten et al.

Murai et al taken in view of Gray et al discloses a method for recovering interferon from plants as discussed supra. Velten et al. discloses the use of the agropine (mannopine) promoter in plant transformation to recover bacterial enzymes encoding antibiotic resistance. In the absence of unexpected results it would be obvious to incorporate the promoter disclosed by Velten et al. into the transformation method disclosed by Murai et al taken in view of Gray et al. since each would continue to function in their known and expected manner.

Any inquiry concerning this communication should be directed to David T. Fox at telephone number 703-557-3920.

DTF

FOX:wdh

6/4/87

THOMAS G. WISEMAN
SUPERVISORY PATENT EXAMINER
ART UNIT 127

TO . ;ATE, 9 TOP AND BOTTOM EDGES, SNAP-APART ANC .ARD CARBON

FORM PTO-892 (REV. 3-78) U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE	SERIAL NO.	GROUP ART UNIT	ATTACHMENT TO PAPER NUMBER
NOTICE OF REFERENCES CITED	760,236	127	7
	APPLICANT(S) Goodman et al.		

U.S. PATENT DOCUMENTS

*		DOCUMENT NO.	DATE	NAME	CLASS	SUB-CLASS	FILING DATE IF APPROPRIATE
	A						
	B						
	C						
	D						
	E						
	F						
	G						
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FOREIGN PATENT DOCUMENTS

*		DOCUMENT NO.	DATE	COUNTRY	NAME	CLASS	SUB-CLASS	PERTINENT SHTS. DWG	PERTINENT PP. SPEC.
	L								
	M								
	N								
	O								
	P								
	Q								

OTHER REFERENCES (Including Author, Title, Date, Pertinent Pages, Etc.)

14	R	Velten et al. 1984. EMBO J 3(2): 2723-2730
14	S	Murai et al. 1983. Science 222: 476-482
14	T	Gray et al. 1982. Nature 295: 503-508
14	U	Goodman et al. 1987. Science 236: 48-54

EXAMINER	DATE
David T. Fox	5/23/87

* A copy of this reference is not being furnished with this office action.
(See Manual of Patent Examining Procedure, section 707.05 (a).)

TO .ATE.) TOP AND BOTTOM EDGES, SNAP-APART ANL ARD CARBON

FORM PTO-892 (REV. 3-78) U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE

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	L								
	M								
	N								
	O								
	P								
	Q								

OTHER REFERENCES (Including Author, Title, Date, Pertinent Pages, Etc.)

	R	Herrera-Estrella et al. 1984. Nature 310: 115-120
	S	
	T	
	U	

EXAMINER	DATE
David T. Fox	5/23/87

* A copy of this reference is not being furnished with this office action. (See Manual of Patent Examining Procedure, section 707.05 (a).)